What is claimed is:

1. A method for the prevention or treatment of proliferative diseases, which comprises administering pharmaceutically effective amounts of a combination of:

(a) a VEGF inhibitor compound; and

(b) one or more chemotherapeutic agents selected from the group consisting of:

i. an aromatase inhibitor;

ii. an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist;

iii. a topoisomerase I inhibitor or a topoisomerase II inhibitor;

iv. a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound;

v. a compound targeting/decreasing a protein or lipid kinase activity or a protein or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes;

vi. a bradykinin 1 receptor or an angiotensin II antagonist;

vii. a cyclooxygenase inhibitor, a bisphosphonate, a heparanase inhibitor (prevents heparan sulphate degradation), e.g., PI-88, a biological response modifier, preferably a lymphokine or interferons, e.g., interferon γ, an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways;

viii. an inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor;

ix. a telomerase inhibitor, e.g., telomestatin;

x. a protease inhibitor, a matrix metalloproteinase inhibitor, a methionine aminopeptidase inhibitor, e.g., bengamide or a derivative thereof, or a proteasome inhibitor, e.g., PS-341;

xi. agents used in the treatment of hematologic malignancies or FMS-like tyrosine kinase inhibitors;

xii. an HSP90 inhibitors;

xiii. HDAC inhibitors;

xiv. mTOR inhibitors;

xv. Somatostatin receptor antagonists;

xvi. integrin antagonists;

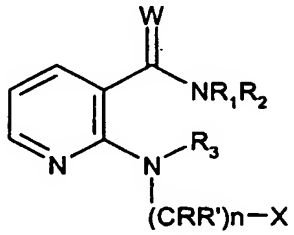
xvii. antileukemic compounds;

xviii. tumor cell damaging approaches such as ionizing radiation;

xix. EDG binders;
xx. anthranilic acid amide class of kinase inhibitors;
xxi. ribonucleotide reductase inhibitors;
xxii. S-adenosylmethionine decarboxylase inhibitors;
xxiii. antibodies against VEGF or VEGFR;
xxiv. photodynamic therapy;
xxv. angiostatic steroids;
xxvi. implants containing corticosteroids;
xxvii. AT1 receptor antagonists; and
xxviii. ACE inhibitors.

2. The method according to claim 1, wherein the VEGF inhibitor compound is

(i) of the formula (I)



(I)

wherein

n is from 1 up to and including 6;

W is O or S;

R_1 and R_3 represent independently of each other hydrogen, lower alkyl or lower acyl;

R_2 represents an cycloalkyl group, an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted;

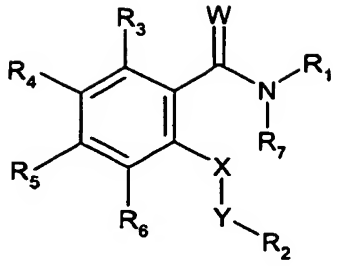
R and R' are independently of each other hydrogen or lower alkyl; and

X represents an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or poly-substituted;

or of an *N*-oxide or a possible tautomer thereof;

or of a pharmaceutically acceptable salt;

(ii) of the formula (II)



(II)

wherein

W is O or S;

X is NR_8;

Y is CR_9R_{10}-$(CH_2)_n$,

wherein

R_9 and R_{10} are, independently, of each other hydrogen or lower alkyl; and

n is an integer of from and including 0 to and including 3; or

Y is SO_2;

R_1 is aryl;

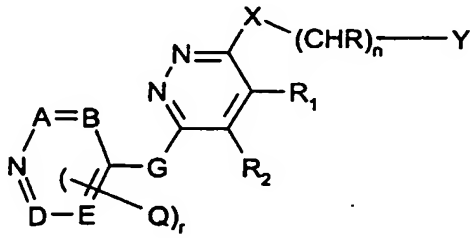
R_2 is a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms with the exception that R_2 cannot represent 2-phthalimidyl, and in case of Y = SO_2 cannot represent 2,1,3-benzothiadiazol-4-yl;

any of R_3, R_4, R_5 and R_6, independently of the other, is H or a substituent other than hydrogen; and

R_7 and R_8, independently of each other, are H or lower alkyl;

or of an *N*-oxide; or a pharmaceutically acceptable salt thereof; or

(iii) of the formula (III)



(III)

wherein

r is 0 to 2,

n is 0 to 2,

m is 0 to 4,

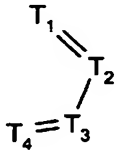
R_1 and R_2 (i) are lower alkyl or

(ii) together form a bridge in subformula (III*)

(III*)

the binding being achieved via the two terminal carbon atoms, or

(iii) together form a bridge in subformula (III**)



(III**)

wherein one or two of the ring members T_1, T_2, T_3 and T_4 are nitrogen, and the others are in each case CH, and the binding is achieved via T_1 and T_4;

A, B, D, and E are, independently of one another, N or CH, with the stipulation that not more than 2 of these radicals are N;

G is lower alkylene, lower alkylene substituted by acyloxy or hydroxy, $-CH_2-O-$, $-CH_2-S-$, $-CH_2-NH-$, oxa (-O-), thia (-S-), or imino (-NH-);

Q is lower alkyl;

R is H or lower alkyl;

X is imino, oxa, or thia;

Y is unsubstituted or substituted aryl, pyridyl, or unsubstituted or substituted cycloalkyl; and

Z is amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherified or esterified hydroxy, nitro, cyano, carboxy, esterified carboxy, alkanoyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower alkylthio, alkylphenylthio, phenylsulfonyl, phenyl-lower alkylsulfinyl or alkylphenylsulfinyl, substituents Z being the same or different from one another if more than 1 radical Z is present;

and wherein the bonds characterized, if present, by a wavy line are either single or double bonds;

or an N-oxide of the defined compound, wherein 1 or more N atoms carry an oxygen atom, or a pharmaceutically acceptable salt of such compound having at least one salt-forming group.

3. The method according to claim 1, wherein the VEGF inhibitor compound is 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine or a pharmaceutically acceptable salt thereof.

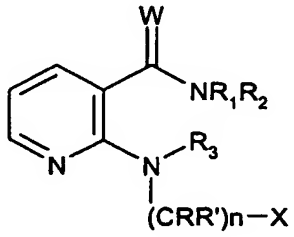
4. The method according to claim 1, which comprises administering pharmaceutically effective amounts of a combination of:

(a) a VEGF inhibitor compound; and

(b) one or more chemotherapeutic agents selected from the group consisting of HDAC inhibitors, microtube active agents, inhibitors or the EGF receptor tyrosine kinase family, mTOR inhibitors, COX-2 inhibitors, ionizing radiation, IGF-IR inhibitors, aromatase inhibitors, bisphosphonates, Bcr-Abl kinase inhibitors, FLT-3 kinase inhibitors, ALK inhibitors, c-Kit inhibitors, platelet-derived growth factor receptor inhibitors, Raf kinase inhibitors, HSP-90 inhibitors, antibodies against VEGF and VEGFR, MMP inhibitors, SRC inhibitors, farnesyl transferse inhibitors and EDG binders.

5. The method according to claim 4, wherein the VEGF inhibitor compound is

(i) of the formula (I)



(I)

wherein

n is from 1 up to and including 6;

W is O or S;

R_1 and R_3 represent independently of each other hydrogen, lower alkyl or lower acyl;

R_2 represents an cycloalkyl group, an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted;

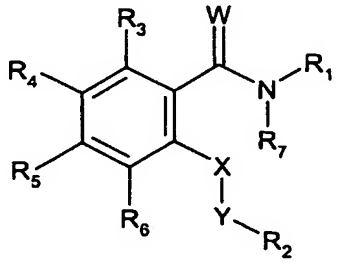
R and R' are independently of each other hydrogen or lower alkyl; and

X represents an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or poly-substituted;

or of an *N*-oxide or a possible tautomer thereof;

or of a pharmaceutically acceptable salt;

(ii) of the formula (II)



(II)

wherein

W is O or S;

X is NR_8;

Y is CR_9R_{10}-$(CH_2)_n$,

wherein

R_9 and R_{10} are, independently, of each other hydrogen or lower alkyl; and

n is an integer of from and including 0 to and including 3; or

Y is SO_2;

R_1 is aryl;

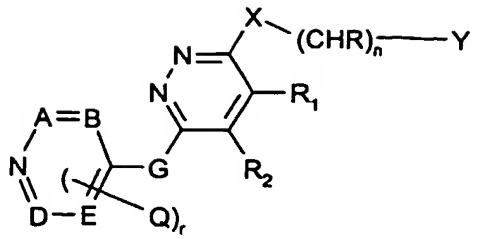
R_2 is a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms with the exception that R_2 cannot represent 2-phthalimidyl, and in case of Y = SO_2 cannot represent 2,1,3-benzothiadiazol-4-yl;

any of R_3, R_4, R_5 and R_6, independently of the other, is H or a substituent other than hydrogen; and

R_7 and R_8, independently of each other, are H or lower alkyl;

or of an *N*-oxide; or a pharmaceutically acceptable salt thereof; or

(iii) of the formula (III)



(III)

wherein

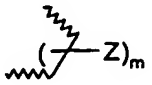
r is 0 to 2,

n is 0 to 2,

m is 0 to 4,

R_1 and R_2 (i) are lower alkyl or

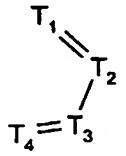
(ii) together form a bridge in subformula (III*)



(III*)

the binding being achieved via the two terminal carbon atoms, or

(iii) together form a bridge in subformula (III**)



(III**)

wherein one or two of the ring members T_1, T_2, T_3 and T_4 are nitrogen, and the others are in each case CH, and the binding is achieved via T_1 and T_4;

A, B, D, and E are, independently of one another, N or CH, with the stipulation that not more than 2 of these radicals are N;

G is lower alkylene, lower alkylene substituted by acyloxy or hydroxy, $-CH_2-O-$, $-CH_2-S-$, $-CH_2-NH-$, oxa (-O-), thia (-S-), or imino (-NH-);

Q is lower alkyl;

R is H or lower alkyl;

X is imino, oxa, or thia;

Y is unsubstituted or substituted aryl, pyridyl, or unsubstituted or substituted cycloalkyl; and

Z is amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy,

etherified or esterified hydroxy, nitro, cyano, carboxy, esterified carboxy, alkanoyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower alkylthio, alkylphenylthio, phenylsulfonyl, phenyl-lower alkylsulfinyl or alkylphenylsulfinyl, substituents Z being the same or different from one another if more than 1 radical Z is present;

and wherein the bonds characterized, if present, by a wavy line are either single or double bonds;

or an N-oxide of the defined compound, wherein 1 or more N atoms carry an oxygen atom,

or a pharmaceutically acceptable salt of such compound having at least one salt-forming group.

6. The method according to claim 4, wherein the VEGF inhibitor compound is 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine or a pharmaceutically acceptable salt thereof.

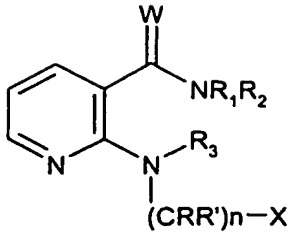
7. The method according to claim 1, which comprises administering pharmaceutically effective amounts of a combination of:

(a) a VEGF inhibitor compound; and

(b) one or more chemotherapeutic agents selected from the group consisting of *N*-hydroxy-3-[4-[[[2-(2-methyl-*1H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, or a pharmaceutically acceptable salt thereof, *N*-hydroxy-3-[4-[(2-hydroxyethyl){2-(*1H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, or a pharmaceutically acceptable salt thereof, epothilones and derivatives thereof, taxanes, discodermolides, vinca alkaloids, colchicines, gefitinib, IGF-IR inhibitors, trastuzumab, RAD001, CCI-779, rapamycin, AP23573, lumiracoxib, celecoxib, valdecoxib, rofecoxib, 5-FU, platin compounds, DNA alkylators, letrozole, anastrozole, exemestane, zoledronic acid, pamidronic acid, imatinib such as especially imatinib mesylate, PD173955, PKC412, MLN518, interferons, Ara-C, bisulfan, SU101, SU6668, GFB-111, BAY43-9006, PD184352, 17-AAG, geldanamycin-related compounds and radicicol.

8. The method according to claim 7, wherein the VEGF inhibitor compound is

(i) of the formula (I)



(I)

wherein

n is from 1 up to and including 6;

W is O or S;

R_1 and R_3 represent independently of each other hydrogen, lower alkyl or lower acyl;

R_2 represents an cycloalkyl group, an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted;

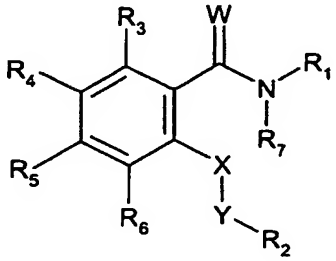
R and R' are independently of each other hydrogen or lower alkyl; and

X represents an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or poly-substituted;

or of an *N*-oxide or a possible tautomer thereof;

or of a pharmaceutically acceptable salt;

(ii) of the formula (II)



(II)

wherein

W is O or S;

X is NR_8;

Y is CR_9R_{10}-$(CH_2)_n$,

wherein

R_9 and R_{10} are, independently, of each other hydrogen or lower alkyl; and

n is an integer of from and including 0 to and including 3; or

Y is SO_2;

R_1 is aryl;

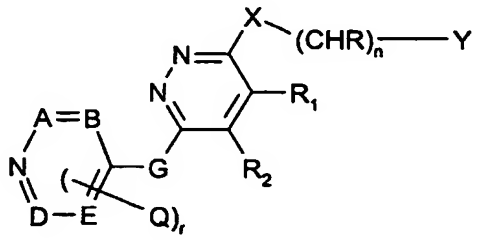
R_2 is a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms with the exception that R_2 cannot represent 2-phthalimidyl, and in case of Y = SO_2 cannot represent 2,1,3-benzothiadiazol-4-yl;

any of R_3, R_4, R_5 and R_6, independently of the other, is H or a substituent other than hydrogen; and

R_7 and R_8, independently of each other, are H or lower alkyl;

or of an *N*-oxide; or a pharmaceutically acceptable salt thereof; or

(iii) of the formula (III)



(III)

wherein

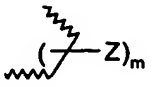
r is 0 to 2,

n is 0 to 2,

m is 0 to 4,

R_1 and R_2 (i) are lower alkyl or

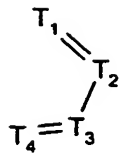
(ii) together form a bridge in subformula (III*)



(III*)

the binding being achieved via the two terminal carbon atoms, or

(iii) together form a bridge in subformula (III**)



(III**)

wherein one or two of the ring members T_1, T_2, T_3 and T_4 are nitrogen, and the others are in each case CH, and the binding is achieved via T_1 and T_4;

A, B, D, and E are, independently of one another, N or CH, with the stipulation that not more than 2 of these radicals are N;

G is lower alkylene, lower alkylene substituted by acyloxy or hydroxy, $-CH_2-O-$, $-CH_2-S-$, $-CH_2-NH-$, oxa (-O-), thia (-S-), or imino (-NH-);

Q is lower alkyl;

R is H or lower alkyl;

X is imino, oxa, or thia;

Y is unsubstituted or substituted aryl, pyridyl, or unsubstituted or substituted cycloalkyl; and

Z is amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherified or esterified hydroxy, nitro, cyano, carboxy, esterified carboxy, alkanoyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower alkylthio, alkylphenylthio, phenylsulfonyl, phenyl-lower alkylsulfinyl or alkylphenylsulfinyl, substituents Z being the same or different from one another if more than 1 radical Z is present;

and wherein the bonds characterized, if present, by a wavy line are either single or double bonds;

or an N-oxide of the defined compound, wherein 1 or more N atoms carry an oxygen atom, or a pharmaceutically acceptable salt of such compound having at least one salt-forming group.

9. The method according to claim 7, wherein the VEGF inhibitor compound is 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition comprising:

(a) a VEGF inhibitor compound; and

(b) one or more chemotherapeutic agents selected from the group consisting of:

i. an aromatase inhibitor;

ii. an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist;
iii. a topoisomerase I inhibitor or a topoisomerase II inhibitor;
iv. a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound;
v. a compound targeting/decreasing a protein or lipid kinase activity or a protein or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes;
vi. a bradykinin 1 receptor or an angiotensin II antagonist;
vii. a cyclooxygenase inhibitor, a bisphosphonate, a heparanase inhibitor (prevents heparan sulphate degradation), e.g., PI-88, a biological response modifier, preferably a lymphokine or interferons, e.g., interferon γ, an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways;
viii. an inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor;
ix. a telomerase inhibitor, e.g., telomestatin;
x. a protease inhibitor, a matrix metalloproteinase inhibitor, a methionine aminopeptidase inhibitor, e.g., bengamide or a derivative thereof, or a proteasome inhibitor, e.g., PS-341;
xi. agents used in the treatment of hematologic malignancies or FMS-like tyrosine kinase inhibitors;
xii. an HSP90 inhibitors;
xiii. HDAC inhibitors;
xiv. mTOR inhibitors;
xv. somatostatin receptor antagonists;
xvi. integrin antagonists;
xvii. anti-leukemic compounds;
xviii. tumor cell damaging approaches, such as ionizing radiation;
xix. EDG binders;
xx. anthranilic acid amide class of kinase inhibitors;
xxi. ribonucleotide reductase inhibitors;
xxii. S-adenosylmethionine decarboxylase inhibitors;
xxiii. antibodies against VEGF or VEGFR;
xxiv. photodynamic therapy;
xxv. angiostatic steroids;

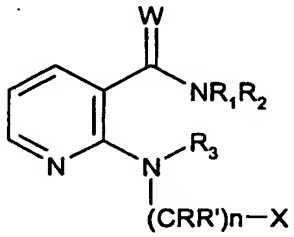
xxvi. implants containing corticosteroids;

xxvii. AT1 receptor antagonists; and

xxviii. ACE inhibitors.

11. The pharmaceutical composition according to claim 10, wherein the VEGF inhibitor compound is

(i) of the formula (I)



(I)

wherein

n is from 1 up to and including 6;

W is O or S;

R_1 and R_3 represent independently of each other hydrogen, lower alkyl or lower acyl;

R_2 represents an cycloalkyl group, an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted;

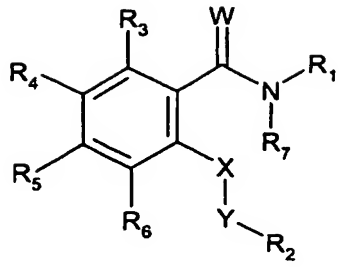
R and R' are independently of each other hydrogen or lower alkyl; and

X represents an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or poly-substituted;

or of an *N*-oxide or a possible tautomer thereof;

or of a pharmaceutically acceptable salt;

(ii) of the formula (II)



(II)

wherein

W is O or S;

X is NR_8;

Y is CR_9R_{10}-$(CH_2)_n$,

wherein

R_9 and R_{10} are, independently, of each other hydrogen or lower alkyl; and

n is an integer of from and including 0 to and including 3; or

Y is SO_2;

R_1 is aryl;

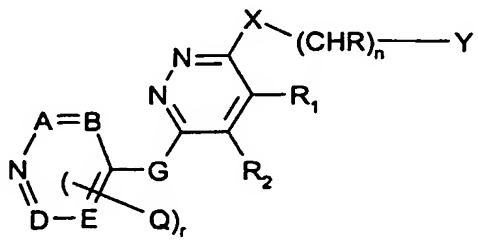
R_2 is a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms with the exception that R_2 cannot represent 2-phthalimidyl, and in case of Y = SO_2 cannot represent 2,1,3-benzothiadiazol-4-yl;

any of R_3, R_4, R_5 and R_6, independently of the other, is H or a substituent other than hydrogen; and

R_7 and R_8, independently of each other, are H or lower alkyl;

or of an *N*-oxide; or a pharmaceutically acceptable salt thereof; or

(iii) of the formula (III)



(III)

wherein

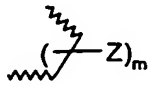
r is 0 to 2,

n is 0 to 2,

m is 0 to 4,

R_1 and R_2 (i) are lower alkyl or

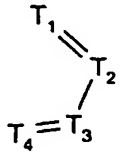
(ii) together form a bridge in subformula (III*)



(III*)

the binding being achieved via the two terminal carbon atoms, or

(iii) together form a bridge in subformula (III**)



(III**)

wherein one or two of the ring members T_1, T_2, T_3 and T_4 are nitrogen, and the others are in each case CH, and the binding is achieved via T_1 and T_4;

A, B, D, and E are, independently of one another, N or CH, with the stipulation that not more than 2 of these radicals are N;

G is lower alkylene, lower alkylene substituted by acyloxy or hydroxy, $-CH_2-O-$, $-CH_2-S-$, $-CH_2-NH-$, oxa (-O-), thia (-S-), or imino (-NH-);

Q is lower alkyl;

R is H or lower alkyl;

X is imino, oxa, or thia;

Y is unsubstituted or substituted aryl, pyridyl, or unsubstituted or substituted cycloalkyl; and

Z is amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherified or esterified hydroxy, nitro, cyano, carboxy, esterified carboxy, alkanoyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower alkylthio, alkylphenylthio, phenylsulfonyl, phenyl-lower alkylsulfinyl or alkylphenylsulfinyl, substituents Z being the same or different from one another if more than 1 radical Z is present;

and wherein the bonds characterized, if present, by a wavy line are either single or double bonds;

or an N-oxide of the defined compound, wherein 1 or more N atoms carry an oxygen atom,

or a pharmaceutically acceptable salt of such compound having at least one salt-forming group.

12. The pharmaceutical composition according to claim 10, wherein the VEGF inhibitor compound is 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine or a pharmaceutically acceptable salt thereof.

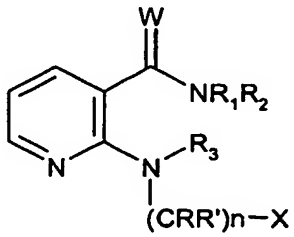
13. The pharmaceutical composition according to claim 10 comprising:

(a) a VEGF inhibitor compound; and

(b) one or more chemotherapeutic agents selected from the group consisting of HDAC inhibitors, microtube active agents, inhibitors or the EGF receptor tyrosine kinase family, mTOR inhibitors, COX-2 inhibitors, ionizing radiation, IGF-IR inhibitors, aromatase inhibitors, bisphosphonates, Bcr-Abl kinase inhibitors, FLT-3 kinase inhibitors, ALK inhibitors, c-Kit inhibitors, platelet-derived growth factor receptor inhibitors, Raf kinase inhibitors, HSP-90 inhibitors, antibodies against VEGF and VEGFR, MMP inhibitors, SRC inhibitors, farnesyl transferse inhibitors and EDG binders.

14. The pharmaceutical composition according to claim 13, wherein the VEGF inhibitor compound is

(i) of the formula (I)



(I)

wherein

n is from 1 up to and including 6;

W is O or S;

R_1 and R_3 represent independently of each other hydrogen, lower alkyl or lower acyl;

R_2 represents an cycloalkyl group, an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted;

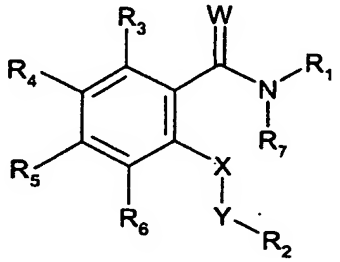
R and R' are independently of each other hydrogen or lower alkyl; and

X represents an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or poly-substituted;

or of an *N*-oxide or a possible tautomer thereof;

or of a pharmaceutically acceptable salt;

(ii) of the formula (II)



(II)

wherein

W is O or S;

X is NR_8;

Y is CR_9R_{10}-$(CH_2)_n$,

wherein

R_9 and R_{10} are, independently, of each other hydrogen or lower alkyl; and

n is an integer of from and including 0 to and including 3; or

Y is SO_2;

R_1 is aryl;

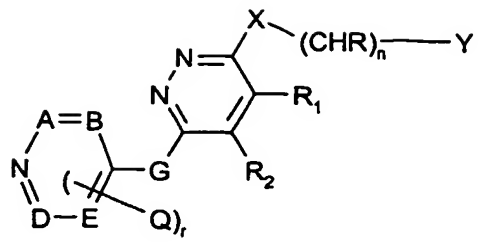
R_2 is a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms with the exception that R_2 cannot represent 2-phthalimidyl, and in case of Y = SO_2 cannot represent 2,1,3-benzothiadiazol-4-yl;

any of R_3, R_4, R_5 and R_6, independently of the other, is H or a substituent other than hydrogen; and

R_7 and R_8, independently of each other, are H or lower alkyl;

or of an *N*-oxide; or a pharmaceutically acceptable salt thereof; or

(iii) of the formula (III)



(III)

wherein

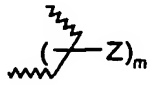
r is 0 to 2,

n is 0 to 2,

m is 0 to 4,

R_1 and R_2 (i) are lower alkyl or

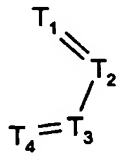
(ii) together form a bridge in subformula (III*)



(III*)

the binding being achieved via the two terminal carbon atoms, or

(iii) together form a bridge in subformula (III**)



(III**)

wherein one or two of the ring members T_1, T_2, T_3 and T_4 are nitrogen, and the others are in each case CH, and the binding is achieved via T_1 and T_4;

A, B, D, and E are, independently of one another, N or CH, with the stipulation that not more than 2 of these radicals are N;

G is lower alkylene, lower alkylene substituted by acyloxy or hydroxy, $-CH_2-O-$, $-CH_2-S-$, $-CH_2-NH-$, oxa (-O-), thia (-S-), or imino (-NH-);

Q is lower alkyl;

R is H or lower alkyl;

X is imino, oxa, or thia;

Y is unsubstituted or substituted aryl, pyridyl, or unsubstituted or substituted cycloalkyl; and

Z is amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy,

etherified or esterified hydroxy, nitro, cyano, carboxy, esterified carboxy, alkanoyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower alkylthio, alkylphenylthio, phenylsulfonyl, phenyl-lower alkylsulfinyl or alkylphenylsulfinyl, substituents Z being the same or different from one another if more than 1 radical Z is present;

and wherein the bonds characterized, if present, by a wavy line are either single or double bonds;

or an N-oxide of the defined compound, wherein 1 or more N atoms carry an oxygen atom, or a pharmaceutically acceptable salt of such compound having at least one salt-forming group.

15. The pharmaceutical composition according to claim 13, wherein the VEGF inhibitor compound is 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine or a pharmaceutically acceptable salt thereof.

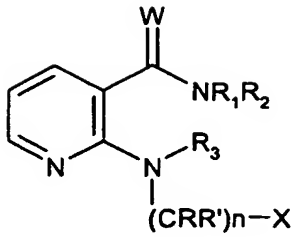
16. The pharmaceutical composition according to claim 10 comprising:

(a) a VEGF inhibitor compound; and

(b) one or more chemotherapeutic agents selected from the group consisting of *N*-hydroxy-3-[4-[[[2-(2-methyl-*1H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, or a pharmaceutically acceptable salt thereof, *N*-hydroxy-3-[4-[(2-hydroxyethyl){2-(*1H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, or a pharmaceutically acceptable salt thereof, epothilones and derivatives thereof, taxanes, discodermolides, vinca alkaloids, colchicines, gefitinib, IGF-IR inhibitors, trastuzumab, RAD001, CCI-779, rapamycin, AP23573, lumiracoxib, celecoxib, valdecoxib, rofecoxib, 5-FU, platin compounds, DNA alkylators, letrozole, anastrozole, exemestane, zoledronic acid, pamidronic acid, imatinib such as especially imatinib mesylate, PD173955, PKC412, MLN518, interferons, Ara-C, bisulfan, SU101, SU6668, GFB-111, BAY43-9006, PD184352, 17-AAG, geldanamycin-related compounds and radicicol.

17. The pharmaceutical composition according to claim 16, wherein the VEGF inhibitor compound is

(i) of the formula (I)



(I)

wherein

n is from 1 up to and including 6;

W is O or S;

R_1 and R_3 represent independently of each other hydrogen, lower alkyl or lower acyl;

R_2 represents an cycloalkyl group, an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted;

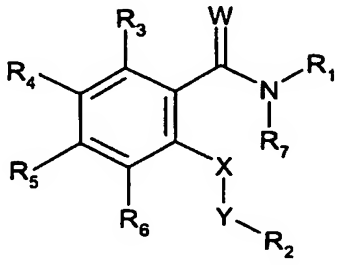
R and R' are independently of each other hydrogen or lower alkyl; and

X represents an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or poly-substituted;

or of an *N*-oxide or a possible tautomer thereof;

or of a pharmaceutically acceptable salt;

(ii) of the formula (II)



(II)

wherein

W is O or S;

X is NR_8;

Y is CR_9R_{10}-$(CH_2)_n$,

wherein

R_9 and R_{10} are, independently, of each other hydrogen or lower alkyl; and

n is an integer of from and including 0 to and including 3; or

Y is SO_2;

R_1 is aryl;

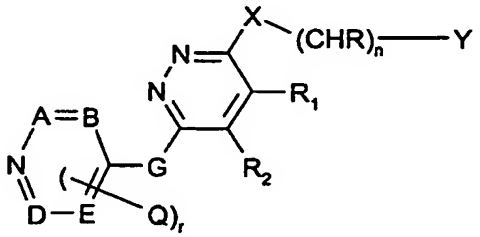
R_2 is a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms with the exception that R_2 cannot represent 2-phthalimidyl, and in case of Y = SO_2 cannot represent 2,1,3-benzothiadiazol-4-yl;

any of R_3, R_4, R_5 and R_6, independently of the other, is H or a substituent other than hydrogen; and

R_7 and R_8, independently of each other, are H or lower alkyl;

or of an *N*-oxide; or a pharmaceutically acceptable salt thereof; or

(iii) of the formula (III)



(III)

wherein

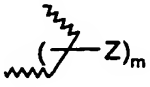
r is 0 to 2,

n is 0 to 2,

m is 0 to 4,

R_1 and R_2 (i) are lower alkyl or

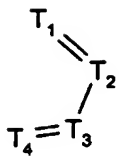
(ii) together form a bridge in subformula (III*)



(III*)

the binding being achieved via the two terminal carbon atoms, or

(iii) together form a bridge in subformula (III**)



(III**)

wherein one or two of the ring members T_1, T_2, T_3 and T_4 are nitrogen, and the others are in each case CH, and the binding is achieved via T_1 and T_4;

A, B, D, and E are, independently of one another, N or CH, with the stipulation that not more than 2 of these radicals are N;

G is lower alkylene, lower alkylene substituted by acyloxy or hydroxy, $-CH_2-O-$, $-CH_2-S-$, $-CH_2-NH-$, oxa (-O-), thia (-S-), or imino (-NH-);

Q is lower alkyl;

R is H or lower alkyl;

X is imino, oxa, or thia;

Y is unsubstituted or substituted aryl, pyridyl, or unsubstituted or substituted cycloalkyl; and

Z is amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherified or esterified hydroxy, nitro, cyano, carboxy, esterified carboxy, alkanoyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower alkylthio, alkylphenylthio, phenylsulfonyl, phenyl-lower alkylsulfinyl or alkylphenylsulfinyl, substituents Z being the same or different from one another if more than 1 radical Z is present;

and wherein the bonds characterized, if present, by a wavy line are either single or double bonds;

or an N-oxide of the defined compound, wherein 1 or more N atoms carry an oxygen atom, or a pharmaceutically acceptable salt of such compound having at least one salt-forming group.

18. The pharmaceutical composition according to claim 16, wherein the VEGF inhibitor compound is 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine or a pharmaceutically acceptable salt thereof.

19. The method of claim 1, wherein the proliferative disease is selected from the group consisting of breast cancer, lung cancer, ovarian cancer, lymphoma, head and/or neck cancer and cancer of the esophagus, stomach, bladder, prostrate, uterus and cervix.